1: Ann Med 1997 Oct;29(5):401-4 Related Articles, Links

Entrez PubMed

PubMed Services

Related Resources

Strategies for identifying and predicting islet autoantigen T-cell epitopes in insulin-dependent diabetes mellitus.

Honeyman MC, Brusic V, Harrison LC.

Autoimmunity and Transplantation Division, The Walter and Eliza Hall Institute, Royal Melbourne Hospital, Victoria, Australia. honeyman@wehi.edu.au

T cells recognize peptide epitopes bound to major histocompatibility complex molecules. Human T-cell epitopes have diagnostic and therapeutic applications in autoimmune diseases. However, their accurate definition within an autoantigen by T-cell bioassay, usually proliferation, involves many costly peptides and a large amount of blood. We have therefore developed a strategy to predict T-cell epitopes and applied it to tyrosine phosphatase IA-2, an autoantigen in IDDM, and HLA-DR4(*0401). First, the binding of synthetic overlapping peptides encompassing IA-2 was measured directly to purified DR4. Secondly, a large amount of HLA-DR4 binding data were analysed by alignment using a genetic algorithm and were used to train an artificial neural network to predict the affinity of binding. This bioinformatic prediction method was then validated experimentally and used to predict DR4 binding peptides in IA-2. The binding set encompassed 85% of experimentally determined T-cell epitopes. Both the experimental and bioinformatic methods had high negative predictive values, 92% and 95%, indicating that this strategy of combining experimental results with computer modelling should lead to a significant reduction in the amount of blood and the number of peptides required to define T-cell epitopes in humans.

PMID: 9453287 [PubMed - indexed for MEDLINE]

1: Bioinformatics 1998;14(2):121-30

Prediction of MHC class II-binding peptides using an evolutionary algorithm and artificial neural network.

Brusic V, Rudy G, Honeyman G, Hammer J, Harrison L.

The Walter and Eliza Hall Institute of Medical Research, PO Royal Melbourne Hospital, Victoria, Australia.

MOTIVATION: Prediction methods for identifying binding peptides could minimize the number of peptides required to be synthesized and assayed, and thereby facilitate the identification of potential T-cell epitopes. We developed a bioinformatic method for the prediction of peptide binding to MHC class II molecules. RESULTS: Experimental binding data and expert knowledge of anchor positions and binding motifs were combined with an evolutionary algorithm (EA) and an artificial neural network (ANN): binding data extraction --> peptide alignment --> ANN training and classification . This method, termed PERUN, was implemented for the prediction of peptides that bind to HLA-DR4(B1*0401). The respective positive predictive values of PERUN predictions of high-, moderate-, low- and zero-affinity binders were assessed as 0.8, 0.7, 0.5 and 0.8 by cross-validation, and 1.0, 0.8, 0.3 and 0.7 by experimental binding. This illustrates the synergy between experimentation and computer modeling, and its application to the identification of potential immunotherapeutic peptides. AVAILABILITY: Software and data are available from the authors upon request. CONTACT: vladimir@wehi.edu. au

PMID: 9545443 [PubMed - indexed for MEDLINE]